Sterne Kessler Goldstein Fox
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August 17, 2004

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Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Art Unit 1654

Re: U.S. Utility Patent Application
Application No. 09/937,484; § 371 Date: January 23, 2002
For: **Use of a Lectin or Conjugates for Modulation of C-Fibre Activity**
Inventors: Foster *et al.*
Our Ref: 1581.0870000/RWE/ALS

Sir:

Transmitted herewith for appropriate action are the following documents:

1. Fee Transmittal (Form PTO/SB/17);

2. Petition to the Director Under 37 C.F.R. §§ 1.144 and 1.181 to Withdraw Final Restriction Requirement;

3. Return postcard; and

4. Credit Card Payment Form PTO-2038 for $130.00 to cover the petition fee.

It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier. In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Aaron L. Schwartz
Agent for Applicants
Registration No. 48,181

ALS/dab
299967_1.DOC
Enclosures

PTO/SB/17 (10-03)
Approved for use through 07/31/2006. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

FEE TRANSMITTAL for FY 2004

Effective 10/01/2003. Patent fees are subject to annual revision.

☐ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 130.00

Complete if Known	
Application Number	09/937,484
Filing Date	January 23, 2002
First Named Inventor	Keith Alan Foster
Examiner Name	Audet, Maury A.
Art Unit	1654
Attorney Docket No.	1581.0870000/RWE/ALS

METHOD OF PAYMENT *(check all that apply)*

☐ Check ☒ Credit card ☐ Money Order ☒ Other** ☐ None

☐ **Deposit Account: **Charge any deficiencies or credit any overpayments in the fees to Deposit Acct. No. 19-0036.

Deposit Account Number: 19-0036

Deposit Account Name: Sterne, Kessler, Goldstein & Fox P.L.L.C.

The Director is authorized to: *(check all that apply)*

☐ Charge fee(s) indicated below ☐ Credit any overpayments

☐ Charge any additional fee(s) or any underpayment of fee(s)

☐ Charge fee(s) indicated below, **except for the filing fee** to the above-identified deposit account.

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1001	770	2001	385	Utility filing fee	
1002	340	2002	170	Design filing fee	
1003	530	2003	265	Plant filing fee	
1004	770	2004	385	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	

SUBTOTAL (1) ($) -0-

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

			Extra Claims		Fee from below		Fee Paid
Total Claims		- 20 **=		X		=	
Independent Claims		- 3 **=		X		=	
Multiple Dependent						=	

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	86	2201	43	Independent claims in excess of 3
1203	290	2203	145	Multiple dependent claim, if not paid
1204	86	2204	43	** Reissue independent claims over original patent
1205	18	2205	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($) -0-

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge - late filing fee or oath	
1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for *ex parte* reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	
1252	420	2252	210	Extension for reply within second month	
1253	950	2253	475	Extension for reply within third month	
1254	1,480	2254	740	Extension for reply within fourth month	
1255	2,010	2255	1,005	Extension for reply within fifth month	
1401	330	2401	165	Notice of Appeal	
1402	330	2402	165	Filing a brief in support of an appeal	
1403	290	2403	145	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive - unavoidable	
1453	1,330	2453	665	Petition to revive - unintentional	
1501	1,330	2501	665	Utility issue fee (or reissue)	
1502	480	2502	240	Design issue fee	
1503	640	2503	320	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	130
1807	50	1807	50	Processing fee under 37 CFR 1.17(q)	
1806	180	1806	180	Submission of Information Disclosure Stmt	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	770	2809	385	Filing a submission after final rejection (37 CFR 1.129(a))	
1810	770	2810	385	For each additional invention to be examined (37 CFR 1.129(b))	
1801	770	2801	385	Request for Continued Examination (RCE)	
1802	900	1802	900	Request for expedited examination of a design application	

Other fee (specify) _____

*Reduced by Basic Filing Fee Paid

SUBTOTAL (3) ($) 130

SUBMITTED BY				(Complete *(if applicable)*)	
Name *(Print/Type)*	Aaron L. Schwartz	Registration No. *(Attorney/Agent)*	48,181	Telephone	(202) 371-2600
Signature				Date	August 17, 2004

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

This collection of information is required by 37 CFR 1.17 and 1.27. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

IFW DAC

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No. 2134
Foster *et al.*	Art Unit: 1654
Appl. No. 09/937,484	Examiner: Audet, Maury A.
§ 371 Date: January 23, 2002	Atty. Docket: 1581.0870000/RWE/ALS
For: **Use of a Lectin or Conjugates for Modulation of C-Fibre Activity**	

Petition to the Director Under 37 C.F.R. §§ 1.144 and 1.181 to Withdraw Final Restriction Requirement

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Sir:

Applicants submit herewith a petition to the director to withdraw a final restriction requirement based on lack of unity of invention. As indicated by 37 C.F.R. §1.499, review of such a petition is provided under 37 C.F.R. §§ 1.144 and 1.181. Further to 37 C.F.R. § 1.181(b), this petition is provided in the following format:

I. Statement of the Facts Involved;

II. Points to be Reviewed; and

III. Action Requested.

The final restriction requirement is based on an allegation that the claims lack unity of invention. Applicants respectfully assert that this restriction requirement is improper and request that it be withdrawn and that all of the claims be examined together. Applicants also request that the claims be examined free of any required election as to specific lectin, peptide, protein, nucleic acid, conjugate, or composition.

I. Statement of the Facts Involved

A. Restriction Requirements

In response to a first restriction requirement mailed October 3, 2003, Applicants provisionally elected to prosecute, **with traverse**, the invention of Group II, represented by claims 39-42 and 47; and the specific conjugate comprising *Erythrina cristagalli* lectin linked to the peptide component inactive $LH_N/A(-)$ of Example 17. *See* Amendment and Reply to Restriction Requirement, filed on November 3, 2003, page 7. Subsequently, the Examiner made a supplemental restriction requirement. *See* Office Action mailed January 29, 2004, beginning on page 3. In response to the supplemental restriction requirement, Applicants provisionally elected, **with traverse**, to prosecute the invention of Group III, represented by claims 39-42, and the specific conjugate comprising *Erythrina cristagalli* lectin. *See* Reply to Restriction Requirement, filed February 27, 2004, page 2. Applicants note that reasons for the traverse were provided in both of the aforementioned replies and are reiterated below. Following Applicants' last reply, the supplemental restriction requirement was made final. *See* Office Action mailed June 21, 2004, page 2, line 12.

B. Pending and Withdrawn Claims

Claims 30-47 (shown below) are pending with claims 30 and 45 being the independent claims. As a result of the restriction requirements and elections, claims 39-42 are subject to examination and claims 30-38 and 43-47 have been withdrawn. *See* Office Action Summary, mailed June 21, 2004.

The pending and withdrawn claims are as follows:

30. (withdrawn) A conjugate comprising a first lectin coupled to a peptide or protein, wherein said first lectin is non-endogenous to humans, and wherein said peptide or protein is substantially free of Clostridial neurotoxin enzyme activity.

31. (withdrawn) A conjugate according to Claim 30 wherein the peptide or protein is a second lectin.

32. (withdrawn) A conjugate according to Claim 30 wherein the first lectin binds to a galactosyl residue.

33. (withdrawn) A conjugate according to Claim 30 wherein the first lectin binds to a glucosyl residue.

34. (withdrawn) A conjugate according to Claim 31 wherein the first and second lectins are different.

35. (withdrawn) A conjugate according to Claim 34 wherein the first lectin binds to a galactosyl residue and the second lectin binds to a glucosyl residue.

36. (withdrawn) A conjugate according to Claim 30, wherein the peptide or protein is an endopeptidase, or a Clostridial neurotoxin substantially free of enzyme activity.

37. (withdrawn) A conjugate according to Claim 30, wherein the first lectin is a lectin derivative, said derivative having been modified to remove a carbohydrate group while maintaining the ability of the derivative to bind C-fibres.

38. (withdrawn) A nucleic acid sequence encoding the conjugate of Claim 30.

39. (previously presented) A method of treating a disease or condition resulting from an inhibition or stimulation of C-fibre neuron activity, by modulating C-fibre activity, comprising administering an effective amount of a lectin, or a nucleic acid sequence coding said lectin, or a conjugate according to Claim 30, or a nucleic acid sequence according to Claim 38, to a patient.

40. (original) A method according to Claim 39 for inhibiting C-fibre activity.

41. (original) A method according to Claim 39 for stimulating C-fibre activity.

42. (original) A method according to Claim 39 wherein said disease or condition is selected from the group consisting of pain, psoriasis, inflammation and mucus hypersecretion.

43. (withdrawn) A method of preparing a conjugate according to Claim 30, comprising coupling together, optionally via a linker, the first lectin and the peptide or protein.

44. (withdrawn) A method of preparing a conjugate according to Claim 30, comprising expressing in a host cell a nucleic acid sequence according to Claim 38, optionally including a linker nucleic acid sequence located within said nucleic acid sequence provides a linker molecule between the first lectin and the peptide or protein of the conjugate.

45. (withdrawn) A composition comprising a lectin and a peptide or protein, wherein the peptide or protein is an endopeptidase or a Clostridial neurotoxin free of enzyme activity.

46. (withdrawn) A composition according to Claim 45, wherein the peptide or protein is an LH_N fragment of a Clostridial neurotoxin.

47. (withdrawn) A method of treating a disease or condition resulting from an inhibition or stimulation of C-fibre neuron activity, by modulating C-fibre activity, comprising administering a composition according to Claim 45 to a patient.

C. Supplemental Restriction Requirement

The final restriction requirement is based on the following Groups:

Group I: Claims 30-37, drawn to a conjugate of lectin (non-endogenous to humans) and a peptide/protein (substantially free of Clostridial neurotoxin enzyme activity);

Group II: Claim 38, drawn to a nucleic acid sequence encoding a conjugate of lectin (non-endogenous to humans) and a peptide/protein (substantially free of Clostridial neurotoxin enzyme activity);

Group III: Claims 39-42, drawn to a method of treating a disease or condition comprising administering an effective amount of a lectin;

Group IV: Claims 39-42, drawn to a method of treating a disease or condition comprising administering an effective amount of a nucleic acid sequence coding a lectin;

Group V: Claims 39-42, drawn to a method of treating a disease or condition comprising administering an effective amount of conjugate of lectin (non-endogenous to humans) and a peptide/protein (substantially free of Clostridial neurotoxin enzyme activity);

Group VI: Claims 39-42, drawn to a method of treating a disease or condition comprising administering an effective amount of a nucleic acid sequence encoding a

conjugate of lectin (non-endogenous to humans) and a peptide/protein (substantially free of Clostridial neurotoxin enzyme activity);

Group VII: Claims 43 and 44, drawn to a method of preparing a conjugate of lectin (non-endogenous to humans) and a peptide/protein (substantially free of Clostridial neurotoxin enzyme activity) comprising coupling the compounds together;

Group VIII: Claims 43 and 44, drawn to a method of preparing a conjugate of lectin (non-endogenous to humans) and a peptide/protein (substantially free of Clostridial neurotoxin enzyme activity) comprising expressing in a host cell a nucleic acid sequence capable of encoding said conjugate;

Group IX: Claims 45 and 46, drawn to a lectin and a peptide or protein (as opposed to a conjugate of the two compounds); and

Group X: Claim 47, drawn to a method of treating a disease or condition comprising administering a lectin and a peptide or protein (as opposed to a conjugate of the two compounds).

II. Points to be Reviewed-- Reasons for Traverse

A. Federal Regulations and PCT Administrative Instructions Demonstrate that Restriction is Improper

Applications which entered the national stage from an international application after compliance with 35 U.S.C. § 371 are governed by the Patent Cooperation Treaty

(PCT) concept of "unity of invention": "An international and a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ('requirement of unity of invention')." 37 C.F.R. § 1.475(a). The M.P.E.P. explicitly indicates that "Examiners are reminded that unity of invention (not restriction) practice is applicable in . . . national stage applications submitted under 35 U.S.C. 371." M.P.E.P. §1893.03(d), Eighth ed. (Rev. 2, May 2004). Indeed, an Examiner can only make a restriction requirement in a national stage application when it lacks unity of invention. 37 C.F.R. § 1.499. Because "unity of invention" is unique to the PCT, Examiners must look both to the Federal laws and regulations *as well as* the PCT and its accompanying guidelines or administrative instructions when making restriction requirements based on lack of unity of invention.

U.S. Patent and Trademark Office regulations provide guidance to Examiners in regard to when claims possess unity of invention:

> (a) . . . Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.
>
> (b) An international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combination of categories: . . .
>
> (3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; . . . .

37 C.F.R. § 1.475(a) and (b)(3). Hence, a group of claims that is directed to a product and processes of making and using that product possess unity of invention if all of the claims comprise the same special technical feature that is free of the prior art.

The Administrative Instructions Under the PCT also provide:

> (c) **Independent and Dependent Claims.** Unity of invention has to be considered in the first place only in relation to the independent claims in an international application and not the dependent claims. By "dependent" claim is meant a claim which contains all the features of another claim and is in the same category of claim as that other claim (the expression "category of claim" referring to the classification of claims according to the subject matter of the invention claimed for example, product, process, use or apparatus or means, etc.).
>
> (i) *If the independent claims avoid the prior art and satisfy the requirement of unity of invention, no problem of lack of unity arises in respect of any claims that depend on the independent claims. In particular, it does not matter if a dependent claim itself contains a further invention.* Equally, no problem arises in the case of a genus/species situation where the genus claim avoids the prior art. Moreover, no problem arises in the case of a combination/subcombination situation where the subcombination claim avoids the prior art and the combination claim includes all the features of the subcombination.

Administrative Instructions Under the PCT, Annex B, Part I (emphasis added). Hence, all claims depending upon an independent claim that i) avoids the prior art and ii) satisfies the requirement of unity of invention necessarily possess unity of invention and should be examined together.

Furthermore, the Administrative Instructions Under the PCT provide exemplary guidelines for examiners:

Example 1

Claim 1: A method of manufacturing chemical substance X.

Claim 2: Substance X.

Claim 3: The use of substance X as an insecticide.

Unity exists between claims 1, 2 and 3. The special technical feature common to all the claims is substance X.

Example 17

Claim 1: Protein X.

Claim 2: DNA sequence encoding protein X.

Expression of the DNA sequence in a host results in the production of a protein which is determined by the DNA sequence. The protein and the DNA sequence exhibit corresponding special technical features. Unity between claims 1 and 2 is accepted.

Administrative Instructions Under the PCT, Annex B, Part II.

Here, Applicants have filed a national stage application under 35 U.S.C. § 371 and the above excerpts regulate whether the claims of the captioned application possess unity of invention. Applicants respectfully assert that the final restriction requirement based on lack of unity of invention is improper and must be withdrawn.

All of Applicants' claims possess unity of invention because they contain the same special technical feature which is free of the prior art. The special technical feature of Applicants' claims should be construed as medicinal lectins. This special technical feature is present in both claims 30 and 45, which are the only independent claims. Moreover, these claims satisfy the requirements of unity of invention in that they both avoid the prior art. Indeed, the Examiner did not apply any prior art rejections in the most recent Office Action. *See* Office Action mailed June 21, 2004. Furthermore, claims 31-44 and 46-47 by virtue of their dependent nature necessarily contain all of the features of claims 30 and 45 and must also be deemed to possess

unity of invention. Hence, it is respectfully asserted that claims 30-47 possess unity of invention and must be examined together.

Holding that claims 30-47 possess unity of invention and must be examined together comports with the above described PCT Administrative Instruction Examples. Applicants' claims that recite peptides/proteins and nucleic acid molecules coding therefor are related like claims 1 and 2 of Example 17 shown above. The remaining dependent claims are related like claims 1-3 of Example 1 provided above. Just as the claims in the Administrative Instruction Examples possess unity of invention, Applicants' claims 30-47 possess unity of invention. Because all of the claims are drawn to compositions comprising conjugates of medicinal lectins (or nucleic acids encoding same) or the methods of manufacture or use thereof, unity of invention exists amongst all of the Groups. Hence, claims 30-47 should be examined together.

B. Examination of all of the Claims is not Burdensome

Applicants respectfully point out that the application was considered to have unity of invention during the international phase. Since a search and examination has already been carried out during the international phase, it would place absolutely no burden on the examiner to examine all of the present claims. Moreover, to the extent that Groups I and IX; III-VI and X; and VII and VIII are respectively classified in the same class and subclass, there is no burden in examining these groups together. A search for documents pertinent to one of these groups is likely to be coextensive for a search for any of the other groups. Furthermore, Groups V and X should also be included with Group III as in each case, the additional peptide/protein component is

simply considered a "carrier" or "adjuvant," rather than the therapeutic molecule (i.e., the lectin).

C. Federal Courts Regard Restriction of a Single Claim as Improper

Finally, it is improper to require restriction of a single claim. See, *In re Weber*, 198 U.S.P.Q. 332 (CCPA 1978) and *In re Hass*, 198 U.S.P.Q. 334 (CCPA 1978). These cases make it clear that 35 U.S.C. § 121 does not grant the PTO the authority to refuse to examine a claim that may read on separate inventions. Section 121 only applies to separate inventions claimed in different claims.

Here, the Examiner's restriction of claims 39-42 into four groups (Groups III-VI) and claims 43 and 44 into two groups (Groups VII and VIII) is improper.

D. Additional Responsive Comments to Examiner's Supplemental Restriction Requirement

Applicants respectfully assert that the Examiner misconstrued the special technical feature. In particular, reliance upon US 6,235,313 ("the '313 patent") to defeat "lectin" as a special technical feature is misplaced. Office Action mailed January 29, 2004, page 6, last paragraph. The '313 patent does not describe the use of any lectin as a *medicament*. Rather, the '313 patent describes the use of microspheres for the delivery of drugs or bioactive molecules. Lectins are not mentioned as drugs or bioactive molecules. The '313 patent mentions that targeting of the microspheres may be modified by incorporating lectins as part of the polymer structure of the microspheres. The lectins are not therefore used as a medicament and, as they form an integral part of the microsphere macrostructure, would not be releasable therefrom or capable of exerting any useful medicinal effect.

Applicants also respectfully point out that the Examiner's reference to any alleged "distinctness" of the claims is irrelevant. *See* Office Action mailed January 29, 2004, pages 7-8. Whether related inventions are "distinct" within the meaning of M.P.E.P. §806.05 is irrelevant in a unity of invention analysis. The relevant analysis is described in section **II.A.** above.

The supplemental restriction requirement also states that "[t]he inventions do not contain a distinguishable structure . . . that may be searched. Therefore . . . Applicant is required to elect a specific lectin, peptide, protein, nucleic acid, conjugate, or composition . . . and submit a structure to that [] compound, to which the elected invention will be examined on the merits as drawn to, **and** so that a search of the invention may be undertaken." Office Action mailed January 29, 2004, page 8, lines 12-17, emphasis in original. Applicants respectfully assert that such an election is irrelevant in a unity of invention analysis and should not be required where the claims possess unity of invention. Claims 30-47 possess unity of invention. Hence, these claims must be examined together without any requirement on Applicants' part to limit them by making unnecessary elections.

III. Action Requested

Applicants respectfully request that the final restriction requirement be withdrawn and that all of the claims be examined together. Applicants also request that the claims be examined free of any required election as to specific lectin, peptide, protein, nucleic acid, conjugate, or composition.

Conclusion

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in accompanying documents. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor are hereby authorized to be charged to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Aaron L. Schwartz
Agent for Applicants
Registration No. 48,181

Date: August 17, 2004

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